## AMENDMENTS

**Amendments to the Claims:**

This listing replaces all prior versions and listings of claims in the application:

**Listing of Claims:**

1. (currently amended) A method for selecting a siRNA molecule for a target gene, wherein said siRNA molecule comprises an antisense region that is 19 – 25 nucleotide bases in length and a sense region that is 19 – 25 nucleotide bases in length ~~19 – 25 nucleotide base pairs~~, said method comprising the steps:
   (a) selecting a target gene;
   (b) identifying ~~generating~~ a set of candidate siRNA sequences ~~molecules~~, wherein the antisense region of each of said candidate siRNA sequences ~~molecules comprises an antisense region of at least 19 bases that~~ is at least 79% complementary to a region of the target gene;
   (c) applying a criterion to each of said candidate siRNA sequences ~~molecules~~, wherein the criterion is selected from the group consisting of: (i) the number of A and U nucleotides present in the first five nucleotide positions at the 5' terminus of the antisense region is higher than that present in the last five nucleotide positions at the 3' terminus of the antisense region; (ii) the number of A and U nucleotides present in the first four positions at the 5' terminus of the antisense region is higher than that present in the last four positions at the 3' terminus of the antisense region; (iii) the number of A and U nucleotides present in the first three positions at the 5' terminus of the antisense region is higher than that present in the last three positions at the 3' terminus of the antisense region; (iv) the number of A and U nucleotides present in the first two positions at the 5' terminus of the antisense region is higher than that present in the last two positions at the 3' terminus of the antisense region; and (v) the first 5' position of the antisense region has either an A or U nucleotide and the last 3' position of the antisense region has neither an A nor U nucleotide; and

(d) selecting a candidate siRNA sequence from the set of candidate siRNA sequences ~~molecules~~ of step (b) as ~~said~~ a siRNA sequence for the target gene, if said candidate siRNA sequence satisfies said criterion; and

(e) synthesizing a siRNA molecule for said target gene, wherein said siRNA molecule for said target gene comprises said siRNA sequence for the target gene.

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38. (previously presented) The method according to claim 1, wherein the criterion is: the number of A and U nucleotides present in the first five nucleotide positions at the 5' terminus of the antisense region is higher than that present in the last five nucleotide positions at the 3' terminus of the antisense region.

39. (previously presented) The method according to claim 1, wherein the criterion is: the number of A and U nucleotides present in the first four positions at the 5' terminus of the antisense region is higher than that present in the last four positions at the 3' terminus of the antisense region.

40. (previously presented) The method according to claim 1, wherein the criterion is: the number of A and U nucleotides present in the first three positions at the 5' terminus of the antisense region is higher than that present in the last three positions at the 3' terminus of the antisense region.

41. (previously presented) The method according to claim 1, wherein the criterion is: the number of A and U nucleotides present in the first two positions at the 5' terminus of

the antisense region is higher than that present in the last two positions at the 3' terminus of the antisense region.

42. (currently amended) The method according to claim 1, wherein the criterion is: the first 5' position of the antisense region has either an A or U nucleotide and the last 3' position of the antisense region had neither an A nor U nucleotide.

43. (currently amended) A method for selecting a siRNA molecule for a target gene, wherein said siRNA molecule comprises an antisense sequence that is 19 – 30 nucleotide bases in length and a sense sequence that is 19 – 30 nucleotide bases in length ~~19 – 30 nucleotide base pairs~~, said method comprising the steps:
    (a) selecting a target gene;
    (b) identifying ~~generating~~ a set of candidate siRNA sequences ~~molecules~~, wherein the antisense sequence of each of said candidate siRNA sequences ~~molecules comprises a sense region of 19 – 30 bases, wherein said sense region comprises a sense sequence of 19 bases that~~ is at least 79% ~~similar~~ complementary to a region of the target gene;
    (c) applying to each of said candidate siRNA sequences a set of one or more criteria selected from the group consisting of a ~~the~~ presence of U ~~A~~ at position 1 ~~19~~ of the antisense sequence, a ~~the~~ presence of U ~~A~~ at position 17 ~~3~~ of the antisense sequence, a ~~the~~ presence of A ~~U~~ at position 10 of the antisense sequence, a ~~the~~ presence of U ~~A~~ at position 6 ~~14~~ of the antisense sequence, an ~~the~~ absence of G ~~C~~ at position 1 ~~19~~ of the antisense sequence, an ~~the~~ absence of C ~~G~~ at position 7 ~~13~~ of the antisense sequence, an ~~the~~ absence of A ~~U~~ at position 15 ~~5~~ of the antisense sequence and an ~~the~~ absence of U ~~A~~ at position 9 ~~11~~ of the antisense sequence, wherein said positions are defined in reference to the 5' end of the antisense sequence ~~sense sequence occupies positions 1 – 19 of the sense region, and wherein when said siRNA is 20 – 30 bases pairs, bases that are not within said sense sequence occupy positions 1 to 11 and positions 1 to 11 are located at the 5' end of the sense region~~; and

(d) selecting a candidate siRNA sequence from the set of candidate siRNA sequences ~~molecules~~ of step (b) as ~~said~~ a siRNA sequence for the target gene, if said candidate siRNA sequence satisfies said one or more criteria; and

(e) synthesizing said siRNA molecule for said target gene, wherein said siRNA molecule for said target gene comprises said siRNA sequence for the target gene.

44. (currently amended) The method according to claim 43, wherein the set of one or more criteria includes the presence of U ~~A~~ at position 1 ~~19~~ of the antisense sequence.

45. (currently amended) The method according to claim 43, wherein the set of one or more criteria includes the presence of U ~~A~~ at position 17 ~~3~~ of the antisense sequence.

46. (currently amended) The method according to claim 43, wherein the set of one or more criteria includes the presence of A ~~U~~ at position 10 of the antisense sequence.

47. (currently amended) The method according to claim 43, wherein the set of one or more criteria includes the presence of U ~~A~~ at position 6 ~~14~~ of the antisense sequence.

48. (currently amended) The method according to claim 43, wherein the set of one or more criteria includes the absence of G ~~G~~ at position 1 ~~19~~ of the antisense sequence.

49. (currently amended) The method according to claim 43, wherein the set of one or more criteria includes the absence of C ~~G~~ at position 7 ~~13~~ of the antisense sequence.

50. (currently amended) The method according to claim 43, wherein the set of one or more criteria includes the absence of A ~~U~~ at position 15 ~~5~~ of the antisense sequence.

51. (currently amended) The method according to claim 43, wherein the set of one or more criteria includes the absence of U ~~A~~ at position 9 ~~11~~ of the antisense sequence.

52. (currently amended) The method according to claim 43 further comprising applying one or more additional criteria selected from the group consisting of: a GC content between about 30% and 52%, at least 2 A or U bases at positions 1 –5 ~~15—19~~ of the antisense sequence, and ~~a~~ an internal repeat that is not stable at greater than 50°C, and selecting said candidate siRNA sequence if said candidate siRNA sequence satisfies said one or more additional criteria.

53. (currently amended) The method according to claim 43, wherein said candidate siRNA sequence is selected as said siRNA sequence for the target gene if said candidate siRNA sequence satisfies at least two criteria selected from the group consisting of: the presence of U ~~A~~ at position 1 ~~19~~ of the antisense sequence, the presence of U ~~A~~ at position 17 ~~3~~ of the antisense sequence, the presence of A ~~U~~ at position 10 of the antisense sequence, the presence of U ~~A~~ at position 6 ~~14~~ of the antisense sequence, the absence of G ~~C~~ at position 1 ~~19~~ of the antisense sequence, the absence of C ~~G~~ at position 7 ~~13~~ of the antisense sequence, the absence of A ~~U~~ at position 15 ~~5~~ of the antisense sequence, and the absence of U ~~A~~ at position 9 ~~11~~ of the antisense sequence.

54. (currently amended) The method according to claim 43, wherein said candidate siRNA sequence is selected as said siRNA sequence for the target gene if said candidate siRNA sequence satisfies at least three criteria selected from the group consisting of: the presence of U ~~A~~ at position 1 ~~19~~ of the antisense sequence, the presence of U ~~A~~ at position 17 ~~3~~ of the antisense sequence, the presence of A ~~U~~ at position 10 of the antisense sequence, the presence of U ~~A~~ at position 6 ~~14~~ of the antisense sequence, the absence of G ~~C~~ at position 1 ~~19~~ of the antisense sequence, the absence of C ~~G~~ at position 7 ~~13~~ of the antisense sequence, the absence of A ~~U~~ at position 15 ~~5~~ of the antisense sequence, and the absence of U ~~A~~ at position 9 ~~11~~ of the antisense sequence.

55. (currently amended) The method according to claim 43, wherein in (c) said method comprises applying a set of four or more criteria ~~candidate siRNA is selected as said~~

~~siRNA for the target gene if said candidate siRNA satisfies at least four criteria~~ selected from the group consisting of: the presence of U ~~A~~ at position 1 ~~19~~ of the antisense sequence, the presence of U ~~A~~ at position 17 ~~3~~ of the antisense sequence, the presence of A ~~U~~ at position 10 of the antisense sequence, the presence of U ~~A~~ at position 6 ~~14~~ of the antisense sequence, the absence of G ~~C~~ at position 1 ~~19~~ of the antisense sequence, the absence of C ~~G~~ at position 7 ~~13~~ of the antisense sequence, the absence of A ~~U~~ at position 15 ~~5~~ of the antisense sequence, the absence of U ~~A~~ at position 9 ~~11~~ of the antisense sequence, a GC content between about 30% and 52%, at least 2 A or U bases at positions 1-5 ~~15—19~~ of the antisense sequence, and ~~a~~ an internal repeat that is not stable at greater than 50°C, and in (d) selecting said candidate siRNA sequence as said siRNA sequence for said target gene if said candidate siRNA sequence satisfies said four or more criteria.

56. (currently amended) The method according to claim 43, wherein in (c) said method comprises applying a set of five or more criteria ~~candidate siRNA is selected as said siRNA for the target gene if said candidate siRNA satisfies at least five criteria~~ selected from the group consisting of: the presence of U ~~A~~ at position 1 ~~19~~ of the antisense sequence, the presence of U ~~A~~ at position 17 ~~3~~ of the antisense sequence, the presence of A ~~U~~ at position 10 of the antisense sequence, the presence of U ~~A~~ at position 6 ~~14~~ of the antisense sequence, the absence of G ~~C~~ at position 1 ~~19~~ of the antisense sequence, the absence of C ~~G~~ at position 7 ~~13~~ of the antisense sequence, the absence of A ~~U~~ at position 15 ~~5~~ of the antisense sequence, the absence of U ~~A~~ at position 9 ~~11~~ of the antisense sequence, a GC content between about 30% and 52%, at least 2 A or U bases at positions 1 - 5 ~~15—19~~ of the antisense sequence, and ~~a~~ an internal repeat that is not stable at greater than 50°C, and in (d) selecting said candidate siRNA sequence as said siRNA sequence for said target gene if said candidate siRNA sequence satisfies said set of five or more criteria.

57. (currently amended) The method according to claim 43, wherein in (c) said method comprises applying the following criteria to each of said candidate siRNA sequences ~~said candidate siRNA is selected as said siRNA for the target gene if said candidate~~

~~siRNA satisfies each of the following criteria: a GC content between about 30% and 52%, at least 2 A or U bases at position 15 – 19 of the sense sequence~~, the presence of U ~~A~~ at position 1 ~~19~~ of the antisense sequence, the presence of U ~~A~~ at position 17 ~~3~~ of the antisense sequence, ~~a base other than~~ the absence of G ~~C~~ at position 1 ~~19~~ of the antisense sequence, ~~a base other than~~ the absence of C ~~G~~ at position 7 ~~13~~ of the antisense sequence, and further comprises applying each of the following additional criteria to each of the candidate siRNA sequences: a GC content between about 30% and 52%, at least 2 A or U bases at position 1 –5 of the antisense sequence and an internal repeat that is not stable at a temperature of greater than 50°C, and in (d) selecting said candidate siRNA sequence as said siRNA sequence for said target gene if said candidate siRNA sequence satisfies the criteria of the presence of U at position 1 of the antisense sequence, the presence of U at position 17 of the antisense sequence, the absence of G at position 1 of the antisense sequence, the absence of C at position 7 of the antisense sequence, the GC content between about 30% and 52%, at least 2 A or U bases at position 1 – 5 of the antisense sequence and the internal repeat that is not stable at a temperature of greater than 50°C.

58. (currently amended) The method according to claim 43, wherein in (c) said method comprises applying the criteria of the absence of C at position 7 of the antisense sequence and further comprises applying the criteria of ~~said candidate siRNA is selected as said siRNA for the target gene if said candidate siRNA satisfies each of the following criteria:~~ a GC content of between 30% and 52% and ~~a base other than G at position 13 of the sense sequence~~ in (d) selecting said candidate siRNA sequence as said siRNA sequence for said target gene if said siRNA sequence satisfies both of said criteria of the absence of C at position 7 of the antisense sequence and the GC content of between 30% and 52% .

59. (currently amended) The method according to claim 43, wherein said candidate siRNA sequence is selected as said siRNA sequence for the target gene if said candidate siRNA sequence satisfies each of the following criteria: ~~a base other than~~

the absence of G ~~C~~ at position 1 ~~19~~ of the antisense sequence and ~~a base other than~~ the absence of C ~~G~~ at position 7 ~~13~~ of the antisense sequence.

60. (currently amended) The method according to claim 43, wherein in (c), said method comprises applying the criteria of the absence of C at position 7 and further comprises applying both of the criteria of ~~said candidate siRNA is selected as said siRNA for the target gene if said candidate siRNA satisfies each of the following criteria~~: a GC content of between 30% and 52%, ~~a base other than G at position 13 of the sense sequence~~ and an internal repeat that is not stable at a temperature of greater than 50°C and wherein in (d) selecting said candidate siRNA sequence as said siRNA sequence for said target gene if said siRNA sequence satisfies all of the criteria of the absence of C at position 7 of the antisense sequence, the GC content of between 30% and 52% and the internal repeat that is not stable at a temperature of greater than 50°C .

61. (New) A method for selecting a siRNA sequence for a target gene, wherein said siRNA sequence comprises an antisense region that is 19 – 25 nucleotide bases in length and a sense region that is 19 – 25 nucleotide bases in length, said method comprising the steps:

(a) selecting a target gene;

(b) identifying a set of candidate siRNA sequences, wherein the antisense region of each of said candidate siRNA sequences is at least 79% complementary to a region of the target gene;

(c) applying a criterion to each of said candidate siRNA sequences, wherein the criterion is selected from the group consisting of: (i) the number of A and U nucleotides present in the first five nucleotide positions at the 5' terminus of the antisense region is higher than that present in the last five nucleotide positions at the 3' terminus of the antisense region; (ii) the number of A and U nucleotides present in the first four positions at the 5' terminus of the antisense region is higher than that present in the last four positions at the 3' terminus of the

antisense region; (iii) the number of A and U nucleotides present in the first three positions at the 5' terminus of the antisense region is higher than that present in the last three positions at the 3' terminus of the antisense region; (iv) the number of A and U nucleotides present in the first two positions at the 5' terminus of the antisense region is higher than that present in the last two positions at the 3' terminus of the antisense region; and (v) the first 5' position of the antisense region has either an A or U nucleotide and the last 3' position of the antisense region has neither an A nor U nucleotide; and

(d) selecting a candidate siRNA sequence from the set of candidate siRNA sequences of step (b) as a siRNA sequence for the target gene, if said candidate siRNA sequence satisfies said criterion; and

(e) generating an output comprising said siRNA sequence for the target gene, wherein said output is in a form that is readable by at least one of a human or computer.

62. (new) The method according to claim 61, wherein the criterion is: the number of A and U nucleotides present in the first five nucleotide positions at the 5' terminus of the antisense region is higher than that present in the last five nucleotide positions at the 3' terminus of the antisense region.

63. (new) The method according to claim 61, wherein the criterion is: the number of A and U nucleotides present in the first four positions at the 5' terminus of the antisense region is higher than that present in the last four positions at the 3' terminus of the antisense region.

64. (new) The method according to claim 61, wherein the criterion is: the number of A and U nucleotides present in the first three positions at the 5' terminus of the antisense region is higher than that present in the last three positions at the 3' terminus of the antisense region.

65. (new) The method according to claim 61, wherein the criterion is: the number of A and U nucleotides present in the first two positions at the 5' terminus of the antisense region is higher than that present in the last two positions at the 3' terminus of the antisense region.

66. (new) The method according to claim 61, wherein the criterion is: the first 5' position of the antisense region has either an A or U nucleotide and the last 3' position of the antisense region had neither an A nor U nucleotide.

67. (new) The method according to claim 61, wherein said output is in a form that is readable by a computer.

68. (new) A method for selecting a siRNA sequence for a target gene, wherein said siRNA comprises an antisense sequence that is 19 – 30 nucleotide bases in length and a sense sequence that is 19 – 30 nucleotide bases in length, said method comprising the steps:

(a) selecting a target gene;

(b) identifying a set of candidate siRNA sequences, wherein the antisense sequence of each of said candidate siRNA sequences is at least 79% complementary to a region of the target gene;

(c) applying to each of said candidate siRNA sequences, a set of one or more criteria selected from the group consisting of a presence of U at position 1 of the antisense sequence, a presence of U at position 17 of the antisense sequence, a presence of A at position 10 of the antisense sequence, a presence of U at position 6 of the antisense sequence, an absence of G at position 1 of the antisense sequence, an absence of C at position 7 of the antisense sequence, an absence of A at position 15 of the antisense sequence and an absence of U at position 9 of the antisense sequence, wherein said positions are defined in reference to the 5' end of the antisense seqeunce; and

(d) selecting a candidate siRNA sequence from the set of candidate siRNA sequences of step (b) as said siRNA sequence for the target gene, if said candidate siRNA sequence satisfies said one or more criteria; and

(e) generating an output comprising said siRNA sequence for the target gene, wherein said output is in a form that is readable by at least one of a human or computer.

69. (new) The method according to claim 68, wherein said output is in a form that is readable by a computer.

70. (new) The method according to claim 68, wherein the set of one or more criteria includes the presence of U at position 1 of the antisense sequence.

71. (new) The method according to claim 68, wherein the set of one or more criteria includes the presence of U at position 17 of the antisense sequence.

72. (new) The method according to claim 68, wherein the set of one or more criteria includes the presence of A at position 10 of the antisense sequence.

73. (new) The method according to claim 68, wherein the set of one or more criteria includes the presence of U at position 6 of the antisense sequence.

74. (new) The method according to claim 68, wherein the set of one or more criteria includes the absence of G at position 1 of the antisense sequence.

75. (new) The method according to claim 68, wherein the set of one or more criteria includes the absence of C at position 7 of the antisense sequence.

76. (new) The method according to claim 68, wherein the set of one or more criteria includes the absence of A at position 15 of the antisense sequence.

77. (new) The method according to claim 68, wherein the set of one or more criteria includes the absence of U at position 9 of the antisense sequence.

78. (new) The method according to claim 1, wherein in (b) said antisense region is 100% complementary to said region of said target gene.

79. (new) The method according to claim 43, wherein in (b) said antisense region is 100% complementary to said region of said target gene.

80. (new) The method according to claim 61, wherein in (b) said antisense sequence is 100% complementary to said region of said target gene.

81. (new) The method according to claim 68, wherein in (b) said antisense sequence is 100% complementary to said region of said target gene.

82. (new) The method according to claim 1, wherein said synthesizing comprises chemical synthesis.

83. (new) The method according to claim 1, wherein said synthesizing comprises enzymatic synthesis.

84. (new) The method according to claim 43, wherein said synthesizing comprises chemical synthesis.

85. (new) The method according to claim 43, wherein said synthesizing comprises enzymatic synthesis.